

REMARKS

Applicants thank the Examiner for indicating that the Sequence Listing and CRF are acceptable; for accepting the Oath and Declaration; for accepting and considering the January 9, 2006 and October 25, 2007 Information Disclosure Statements and the documents cited therein; and for granting the July 9, 2003 priority claim.

The Claim Amendments

Applicants have canceled claims 51, 56-57, 60, 63, 68, 72 and 84-85. Claims 45-50, 52, 55, 58-59, 61-62, 64-67, 69-71 and 73-83 remain pending.

Applicants have amended the two remaining independent claims (claims 45 and 52) and, thus, all of the remaining dependent claims to recite treating a respiratory disease by administering in the form of a dry powder a composition comprising a double-stranded oligonucleotide of SEQ ID NO:1 or 3 and their complements in a naked form and one or more excipients directly to the respiratory system. This amendment is supported throughout the application. *See, e.g.*, 12:10-24 (an NF-KB decoy for treating a respiratory disease); 13:31-32, 22:10-17, 24:19-25:9 and 58:19-33 (SEQ ID NO:1 and 3); 15:26-29 and 41:9-16 (dry powder); 54:10-25 (excipients); and 54:1-5 and 63:10-13 (naked form).

Applicants have also amended various of the dependent claims to be consistent with amended independent claims 45 and 52. These amendments are also supported in the application as filed and in the original claims. *See, e.g.*, 16:27-31 and 19:16-20 (nasal drop, nasal spray agent, nebulizer, respirator, and powder

administration formulation) (claims 50 and 67); 25:10-19 (thiophosphatediester and substituted with a methylphosphate group) (claims 55 and 59); and 64:8-19 (lactose and light anhydrous silicic acid (claims 58 and 64).

Applicants have made the recited claim cancellations and claim amendments without prejudice to their right to seek patents on the deleted and canceled subject matter in this application or in applications claiming the benefit and priority hereof.

The Claim Objections

Claim 50 stands objected to for the informality "Into". Applicants have amended the claim to put it in proper form.

Claims 55 and 60 stand objected to for the informality of "NP-KB". Applicants have amended claim 55 to avoid the informality and have canceled claim 60.

Claim 55 also stand objected to as being in improper dependent form. Applicants have amended claim 55 to make it properly dependent on claim 45. It further limits the oligonucleotide of claim 45.

Claim 71 stands objected to for the informality "O,l". Applicants have amended the claim to be in correct decimal form.

The Rejections

a) 35 U.S.C. § 112 – Written Description

Claims 45-52 and 55-85 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement.

In particular, the Examiner has rejected claim 45 because it recites administering a genus of NF-KB decoys and the working examples are allegedly directed to two decoys (SEQ ID NOS:1 and 3), which decoys the Examiner acknowledges are described.

Solely to advance prosecution and without prejudice, applicants have amended claims 45 and 52, the only independent claims remaining in this application, to recite oligonucleotides having a sequence of SEQ ID NOS: 1 or 3 and complements thereof. In view of this amendment, applicants request reconsideration and withdrawal of the written description rejection.

b) 35 U.S.C. § 112 – Enablement

Claims 45-52 and 55-85 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. In particular, the Examiner has rejected the claims because they recite “preventing” a respiratory disease while the working examples allegedly are limited to “treating” such diseases, which treatment the Examiner agrees is enabled.

Solely to advance prosecution and without prejudice, applicants have amended claims 45 and 52, the only remaining independent claims, to recite “treating” respiratory diseases. In view of this amendment, applicants request reconsideration and withdrawal of the enablement rejection.

c) **35 U.S.C. § 102 – Anticipation**

Claims 45-47, 52, 55 and 59 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lee (*FASEB Journal*, 2001, 15:pA663, #523.9) ("*Lee*"). Applicants traverse.

The Examiner contends that *Lee* teaches the administration of NF-KB p65 antisense oligonucleotides to an asthmatic mouse model and suggests that a strategy to inhibit airway NF-KB activity may be beneficial in the treatment of respiratory allergic diseases. The Examiner then argues that the rejected claims using "any oligonucleotides" and, thus, *Lee*'s antisense oligonucleotides are not novel over *Lee*. Applicants traverse.

Applicants have amended claims 45 and 52, the only remaining independent claims, to recite oligonucleotides having the sequence of SEQ ID NOS:1 and 3 and their complements. The *Lee* NF-KB p65 antisense oligonucleotide is not an oligonucleotide of SEQ ID NO: 1 or 3 or their complements. Further, antisense oligonucleotides are single-stranded. Claims 45 and 52 recite double-stranded oligonucleotides. For both reasons, *Lee* does not anticipate the amended claims. Applicants request that the Examiner reconsider and withdraw the anticipation rejection.

d) **35 U.S.C. § 103 – Obviousness**

Claims 45-52 and 55-85 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over *Lee* in view of Morishita United States patent 6,262,033 ("*Morishita*") and further in view of Debs United States patent 5,641,662 ("*Debs*")

and further in view of Cutie United States patent 6,464,959 ("*Cutie*"). Applicants traverse.

As demonstrated above, *Lee* does not describe or teach using a double-stranded oligonucleotide having the sequence of SEQ ID NO:1 or 3 or their complements. None of *Morishita*, *Debs* or *Cutie* remedy that defect in the primary document *Lee*.

Morishita refers to SEQ ID NO:1. However, it does not suggest that an NF-KB decoy of SEQ ID NO:1 would be useful in treating a respiratory disease. Rather, *Morishita* recites that asthma, among many other diverse diseases, may be related to the over expression or under expression of one or a few of a set of unidentified proteins. *Morishita* goes on to recite that a variety of transcriptional regulatory factors, including NF-KB, are generally involved in the expression of proteins. There is no suggestion that NF-KB is involved in asthma or that an NF-KB decoy should be used to treat asthma. Indeed, the opposite is true. *Morishita* recites several diseases that are said to be NF-KB associated diseases. See 1:54 – 2:17. None is a respiratory disease. Accordingly, *Morishita* does not remedy the defect in *Lee* so as to render the amended claims unpatentable. Further, there is no suggestion in either *Lee* or *Morishita* that the decoy of SEQ ID NO:1 could be substituted for the antisense DNA of *Lee*.

Debs recites treating respiratory disease using airway delivery. *Debs* says nothing about treating respiratory disease with NF-KB decoys, much less the ones of SEQ ID NOS:1 and 3 and their complements. Nor does *Debs* suggest that

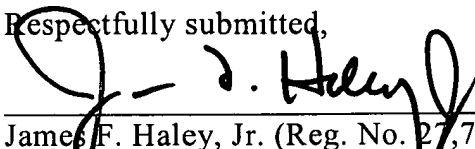
such decoys could be delivered to the airway and be effective in treating respiratory diseases. Indeed, at best *Debs* recites using a conjugate of an nucleic acid that encodes a protein. Such conjugate is not a naked DNA. It is also not an NF-KB decoy. Such decoys do not encode proteins. Thus, *Debs* even in combination with *Lee* and *Morishita* does not render the amended claims unpatentable.

Cutie recites the powder delivery of drugs. Like *Debs*, *Cutie* says nothing about the use of NF-KB in treating respiratory disease. Nor does *Cutie* suggest that NF-KB decoys could be delivered to the airway in powder form and be effective in treating respiratory diseases. Thus, *Cutie*, even in combination with *Lee*, *Morishita* and *Debs*, does not render the amended claims unpatentable.

CONCLUSION

For all of the above reasons, applicants request that the Examiner reconsider and withdraw the pending rejections and allow the amended claims.

Respectfully submitted,


James F. Haley, Jr. (Reg. No. 27,794)

Attorney for Applicants

ROPES & GRAY LLP

(Customer No. 1473)

1211 Avenue of the Americas

New York, New York 10036

Tel.: (212) 596-9000

Fax.: (212) 596-9090